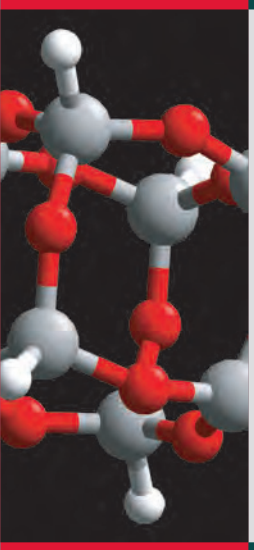


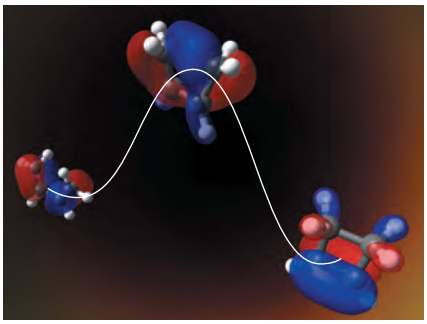
# Jaguar

## A rapid ab initio electronic structure package

Jaguar is a high-performance ab initio package for both gas and solution phase simulations, with particular strength in treating metal-containing systems, making it the most practical quantum mechanical tool for solving real-world problems.

SCHRÖDINGER.

## The Advantages of ab initio Quantum Mechanics

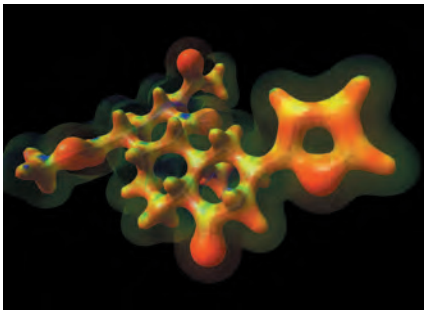


Transition states reveal important information about reaction mechanisms and kinetics, but are often difficult to characterize precisely. Jaguar's transition state calculations converge quickly and reliably, and can be conveniently set up from the Maestro interface.

Even with tremendous advances in molecular mechanical methods, there remain important research questions that cannot be answered without examining in detail a molecule's electronic structure. Also, molecular mechanics methods are limited by their parametrization. For example, conventional force fields either fail to treat metal-containing systems, or experience large errors in computed results. High-level quantum mechanics is still the most accurate and most direct way to study these challenging systems, despite the increased computational cost.

An efficient quantum mechanical program is indispensable to the complete arsenal of any researcher who is interested in reactive chemistry, systems containing transition metals, or phenomena that require precise energetics.

## Jaguar: Maximizing Returns in Real-World Research

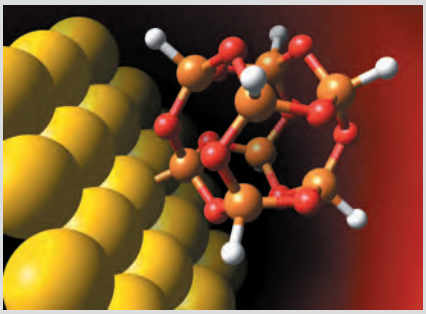


The electron density surface of an organic molecule is shown above colored according to the electrostatic potential. Visualization of electronic properties makes it possible to identify electrophilic and nucleophilic regions of the molecule.

Schrödinger's Jaguar is an extremely fast quantum mechanics package. It provides the following benefits:

- **High performance:** Jaguar proceeds much faster than conventional ab initio programs, making it possible to carry out many more calculations within the same time frame.
- **Real-world systems:** Jaguar scales well with molecular size, allowing it to be applied to larger, real-world problems without having to unrealistically reduce the size of the chemical system under study.
- **Higher accuracy:** Jaguar's performance advantage makes possible the application of higher levels of theory, resulting in more accurate energies and properties. Jaguar models important solvent effects by applying a self-consistent reaction field (SCRF).
- **Chemical properties:** Jaguar computes a comprehensive array of molecular properties including NMR, IR, $pK_a$, partial charges, multipole moments, polarizabilities, molecular orbitals, electron density, electrostatic potential, Mulliken population, and NBO analysis.
- **Potential energy surface:** Jaguar maps reaction coordinates between reactants, products, and transition states; Jaguar also generates potential energy surfaces with respect to variations in internal coordinates.
- **Easy-to-use interface:** Jaguar accepts a wide variety of input formats. Calculations are easily set up and results visualized using the Maestro user interface. Jaguar also provides batch processing, ensuring consistent calculational protocol across all molecular systems being examined.

## Performance-Driven Technology

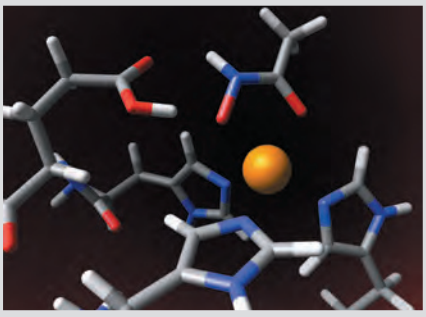


Jaguar's unique transition metal initial guess makes it possible to accurately predict structures and vibrational frequencies that are in excellent agreement with experiment for systems like the siloxane cluster on a gold surface shown above.

Jaguar's performance advantages are built on superior technology:

- **Pseudospectral method**: A modified version of the pseudospectral method, a numerical approach widely used in hydrodynamic simulations, is incorporated into Jaguar to solve the equations of electronic structure theory, making Jaguar calculations much faster than conventional methods. Furthermore, the pseudospectral method scales better with molecular size than conventional methods, making Jaguar's performance advantage even larger as the size of the system increases.
- **SCRF model**: Jaguar uses a Poisson-Boltzmann solver in its self-consistent reaction field (SCRF) calculations to simulate the solvent environment. Jaguar's SCRF model includes short-range corrections to dielectric continuum theory, and demonstrates excellent agreement with experiments in computed solvation free energies.
- **Transition metal initial guess (TMIG):** Jaguar consistently converges to the correct ground state for transition metal-containing systems by employing an initial guess wavefunction that uses the best set of linear combinations of valence orbitals with maximum bonding character.
- **Model wavefunctions**: Jaguar includes Hartree-Fock (HF), Density Functional Theory (DFT), Generalized Valence Bond (GVB), and second-order Møller-Plesset perturbation theory (MP2). Jaguar also includes Time-dependent Density Functional Theory (TDDFT) for studying excited states. Jaguar provides several new density functionals, some unavailable in other packages: X3LYP, MPW1K, MPW1PW91.
- **User-contributed technology**: Jaguar enjoys a vast community of users, among them leading scientists of great renown. Jaguar routinely incorporates new technologies contributed by users to maintain the state-of-the-art in high-performance quantum mechanics.

## Tumor Necrosis Factor-α Converting Enzyme (TACE) Inhibitors



Acetohydroxamic acid, one of the inhibitors studied by researchers at Schering-Plough, is shown above complexed to the zinc ion and the Glu-406 residue in the TACE active site.

Tumor necrosis factor-α converting enzyme (TACE) is a zinc endopeptidase that releases soluble tumor necrosis factor-α (TNF-α) from its membrane-bound precursor. TNF-α is implicated in many diseases: rheumatoid arthritis, diabetes, endotoxic shock, HIV cachexia, cardiac dysfunction in myocarditis, osteoarthritis, and others; which is why effective inhibition of TACE is of great pharmaceutical interest.

Understanding the binding process in detail is essential in designing effective inhibitors. Scientists at Schering-Plough Research Institute applied Jaguar to compute the microscopic $pK_a$ values within the TACE active site as different model inhibitor ligands bound to the zinc ion in the binding cavity. The $pK_a$ values of acidic protons in proteins are difficult to measure experimentally; with results computed by Jaguar, the researchers were able to propose a detailed mechanism of inhibitor binding and subsequent proton transfer, which is consistent with all available experimental observations.

Cross, J.B.; Duca, J.S.; Kaminski, J.J.; and Madison, V.S. *JACS*, **2002**, *124*, 11004-11007.

## Evaluation Copies

To request an evaluation copy of Jaguar, please contact info@schrodinger.com. Our staff of support scientists will be happy to assist you in giving Jaguar a thorough trial.

# Jaguar

**A rapid ab initio electronic structure package**

## A Coordinated Family of Products

In addition to Jaguar, Schrödinger offers MacroModel, a general-purpose molecular mechanics program with wide applicability across a diverse range of chemical systems.

QSite, a mixed QM/MM program, takes advantage of Jaguar to perform the QM calculations while treating the non-critical region with molecular mechanics, making it an efficient program for studying reactions in active sites of large biological systems.

All Schrödinger products are seamlessly integrated through the Maestro graphical interface.

## Additional Information:

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